

REMARKS

Claims 3-8, 33 and 36 remain in the application for further prosecution. Claim 33 has been amended to clarify the invention relative to the cited references and includes additions suggested by the Examiner. In particular, an inlet port and capillary passageway have been included and the structures have been defined so as to emphasize the difference between the device of the Applicants and that of Buechler. Claims 40 and 41 have been added. Claim 40 finds support in the vent 38 of Figs. 3/4, which clearly is located after the microstructure. Claim 41 finds support in inlet port 30 of Figs. 3/4, which can serve as a vent for air after liquid has entered the well 32/34 and moved over the microstructures.

Claim 39 has been withdrawn on his own initiative by the Examiner as a non-elected invention. However, under 37 C.F.R. 1.145 this action is subject to reconsideration and appeal. Accordingly, the Applicants request reconsideration. The broad “means” clause is construed according to 35 U.S.C. 112 “*to cover the corresponding structure...described in the specification and equivalent thereof*”. Thus, the structures of claim 33 and dependent claims 3-8 and 36 are already incorporated in Claim 39.

Rejection Under 35 USC 103(a)

Claims 3, 5, 6, 33 and 36 have been rejected again as unpatentable (i.e. obvious) over Buechler (U.S. 6,133,855) in view of Hillman et al. (U.S. 4,756,884).

As the Examiner says, the microfluidic device disclosed by Buechler has features in common with the Applicant’s device. However, the Examiner’s description is puzzling in referring to a “*substrate surface comprising an array of post structures...that is also positioned adjacent to the substrate*”. Buechler is unclear when discussing reagents (see column 4, lines 42-67). It is not possible to understand exactly where Buechler would place reagents. But, the

Applicants believe that Buechler would place reagents on the posts in order to increase reaction rates, since his capillary space “*should be as small as possible to improve the kinetics of the reaction*” (column 4, lines 56-58). In contrast, the Applicants claim that their reagents (or conditioning agents) are deposited on an absorbent substrate positioned adjacent to the array of posts. The substrate may be above the posts or below the posts or in contact with the top of the posts, but inherently would not block the spaces between the posts where liquid must flow. Therefore, Buechler must be considered to differ structurally in the location of reagents relative to the posts. The Examiner concedes that “*Buechler does not specifically teach a reagent deposited on an absorbent substrate...positioned adjacent to the uniform array of posts*”.

The Examiner notes that “*Buechler does teach the incorporation of surface bound reagents...on a solid phase within region 16*”. However, Buechler says very little in that regard. One must deduce from his ambiguous comments how Buechler would place his reagents. His remarks appear to relate to both liquid or solid reagents. As he says “when an assay requires binding of reactants to a solid phase, the capillary space should be as small as possible to improve the kinetics of the reaction” (emphasis supplied) (column 4, lines 56-58). From this, the Applicant’s conclude that Buechler was thinking of binding reagents directly to the posts in the distal region. There is no indication that Buechler would place reagents on an absorbent substrate adjacent the posts.

Most importantly, Buechler teaches that his posts must provide a capillary force that is greater than (or similar to) the capillary force in his inlet capillary. He devotes significant space to explaining why, in his opinion, the inlet chamber is so designed (see column 5, line 54 to column 6, line 5). It is the desired capillary force in the distal region relative to the capillary force in the proximal region that determines the dimensions of both the capillary and the inlet

chamber. Buechler creates a desired capillary force in the distal region by adding an array of posts, which allows liquid to flow while making the distal region compact and not elongated. In contrast, the Applicant's device employs an absorbent substrate in the distal region and reduces capillary force relative to the proximal region.

Examiner relies on the KSR case to supply deficiencies of Buechler or Hillman. The teachings of Hillman are ambiguous at best. Hillman does show a device in his Fig. 1A that could be similar to those of Buechler and the Applicants, in that a capillary passageway supplies a wider area containing reagents. In discussing Fig. 1A, Hillman says the reagents are dried on the surface (column 18, lines 16-32). Hillman says nothing about structures in the wider region (20 in Fig. 1), so one must assume that liquid entering region 20 is free to fill the region as it will. It might trap air bubbles by traveling along the side walls and thus not contact all of the reagents on the surface. But, if a reagent-containing substrate were to be added to region 20 it should be evident that obtaining uniform contact with the substrate would be more difficult, since the substrate presents an obstacle that could hinder the flow of liquid. Furthermore, if the reagent-containing substrate is fibrous in nature, substantial capillary forces would be created and they would also affect the flow of liquid.

Although Hillman evidently preferred to deposit reagents on the surface of the chamber (column 16, lines 9-12), he mentioned other possible means for introducing reagents, including a vial containing or encapsulating the reagent (as liquid). Even when Hillman suggests locating a reagent on a separate surface (column 16, lines 55-61) various surfaces are suggested, he states that "*In this manner the fluid may pass through the foam structure dissolving the reagent so as to form the reaction mixture*". Thus, Hillman had in mind releasing the reagent to combine with the sample. In contrast, the Applicants were concerned with distributing a sample

uniformly over their substrate, where a reaction occurs. The accuracy of results is affected by whether the reagent sees a uniform portion of the sample. Thus, the many means of disposing reagents mentioned by Hillman leave one skilled in the art with no way to reach the configuration of the Applicant's device.

The Examiner states as his reasoning "*it would have been obvious to a person of ordinary skill in the art to substitute and incorporate a reagent-containing absorbent substrate with the disclosed microfluidic device in order to facilitate effective sample fluid flow control and subsequent testing.*" The Applicants disagree. The Examiner merely combines elements of the Applicant's invention, after having seen it described, and concludes it would have been obvious to do so. If so, then the Buechler and Hillman patents make any subsequently improved microfluidic devices so obvious that they could easily be made by those skilled in the art. Consequently, there would have been no need for continued research and development, as was done by the Applicants in arriving at the present invention. Such a conclusion is obviously absurd, since the structure and its function are related. If one considers the problems being addressed and the means found to solve them, it should be clear that improvements will be found that are not evident in the view of the state of the art.

Buechler improves contact with reagents disposed in his distal region by locating the reagents on the surface of posts, which limit the space available for liquid flow and by increasing liquid velocity raise the effective capillarity. If successful, as Buechler teaches it is, there is no reason to place the reagent on a separate substrate and separate the substrate from the posts. Nor would it be obvious to space the posts so as to lower the effective capillarity and reduce the liquid velocity, thereby obtaining uniform contact with the substrate. In other words, why would one skilled in the art make such changes to the Buechler design?

If one wanted to place their reagents on a substrate, it would seem that one would follow Buechler's lead by wrapping the substrate around posts to achieve the alleged advantage of increased liquid velocity. Thus, the substrate would be uniformly contacted and expected to achieve good results. However, if the substrate is *not* wrapped around the posts, it could be placed in various locations, with and without posts. But, the results would not be predictable and testing would be required. In the absence of the present disclosure, one skilled in the art could not predict whether placing the reagent-containing substrate adjacent a set of posts disposed to both direct fluid flow and reduce the effective capillarity would provide good results. Not only would there be no motivation to do so, but such arrangements are no more than something to try.

The claimed microfluidic device is inherently more complex than the device at issue in the KSR case. In KSR, a single Jepson claim stated that it was an improvement to an adjustable accelerator pedal to place an electronic throttle connection on a fixed pivot. Since the advantage of avoiding movement of the throttle connection was considered obvious, the claim was determined to be invalid. Unfortunately, the court took the opportunity to expand the scope of obviousness, including the question of obvious to try. The court assumed where "*there are a finite number of identified, predictable solutions a person of ordinary skill in the art has a good reason to pursue the known options within his or her technical grasp*" (emphasis added). The court further relied on the "common sense" of one skilled in the art. However, these considerations may have applied to the KSR accelerator pedal, they lose their force when microfluidic technology is the subject.

An important question with respect to obvious to try is one of predictability. That is, if a group of possible solutions to a problem can be listed, it may not be evident that any of the potential solutions will be successful. The Applicant's problem was how to distribute a

liquid sample uniformly over a reagent-containing substrate in an enclosed space, while expelling air. Trapping air would prevent achieving the desired uniform response of the reagent. Using an array of posts in a manner contrary to Buechler should not be considered obvious to try and could not be predicted to be successful without experimental evaluation.

The Examiner notes that Hillman suggests that the reagents can be disposed on an absorbent substrate. Hillman does not discuss how or where such reagent-containing substrates would be deployed. Furthermore, Hillman does not suggest using posts or other structures to assist in distributing liquid samples. The Examiner must jump to the conclusion that it would be obvious to add the substrate of Hillman to the Buechler device, but without any reason other than quoting from the KSR opinion.

The Examiner appears to infer that any combination of references may be made without providing a motivation to do so. However, the Examiner should make clear his reasons for concluding that Hillman would have led one of ordinary skill in the art to place a reagent (or conditioning agent) – containing substrate adjacent the array of posts used by Beuchler so that uniform contact of a sample with the substrate is achieved. The discussion above provides reasons why one skilled in the art would not have made such a combination.

In his declaration under 37 CFR 1.132, dated April 10, 2007, Dr. Pugia demonstrated that the combination of a porous substrate positioned adjacent an array of microposts was necessary to prevent bypassing of liquid along the chamber walls, which traps air and prevents uniform distribution over the substrate. A copy of that declaration is enclosed, including color photos that make it easier to follow Dr. Pugia's description. The Examiner is asked to review this declaration, since it demonstrates the importance of the claimed device in achieving the Applicant's purpose. Furthermore, since the references do not include all of the

elements of the Applicant's device, the reference elements would not produce the results achieved by the Applicants. Even if the references included all the Applicant's elements, there are no teachings that would enable one skilled in the art to combine them as in the presently claimed device.

Dependent claims 3-8 and 36 should be allowable if, as the Applicants contend, independent Claim 33 is patentable over Buechler in view of Hillman.

Claim 3 adds a second column of posts which, as the Examiner notes, is shown by Buechler.

Claim 5, 6, and 36 cover alternatives in which the location of the absorbent substrate is specified. As previously discussed, the location of an absorbent substrate is not obvious unless one considers "obvious to try" to render any and all location to be obvious. However, success is not predictable in the development of microfluidic devices.

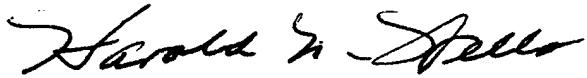
Claim 4 was rejected under 35 USC 103(a) as unpatentable over Buechler and Hillman, in view of Peters. Again, the Examiner relied on KSR to support his rejection. While Claim 4 is only dependent from Claim 33 and should be patentable, it has been previously pointed out that Peters taught the use of posts with wedge-shaped cutout in a different manner than they are used in the Applicant's design. Peters empties capillaries with his cutouts, while in the Applicant's inventions the cutouts are positioned 90° from the direction of liquid flow.

Claims 7 and 8 were rejected under 35 USC 103(a) as unpatentable over Buechler and Hillman in view of Columbus, who is cited for teaching ramp structures, again relying on KSR. Claims 7 and 8 are dependent from Claim 33 and also should be allowable. As has been discussed previously, Columbus uses opposed set of grooves to spread liquid in all directions. The Applicants spread liquid across the entrance to the reagent-containing well, which is

structurally and functionally different. Columbus provides no assistance to one skilled in art that leads to the Applicant's device.

The Examiner is urged to allow the newly amended claims. If further amendments are believed necessary, the Examiner is invited to contact the Applicant's attorney at the telephone number provided below.

Respectfully submitted,



Harold N. Wells
Registration No. 26,044

Date:

Kelley Drye & Warren LLP
333 West Wacker Drive
Suite 2600
Chicago, Illinois 60606-3913
Telephone: 312/857-2336